CLAIMS

- 1. (Currently Amended) A <u>computational</u> method of assessing the hepatotoxicity of a stimulus, the method comprising:
- (a) analyzing, with a computational device, an image of hepatocytes that have been exposed to a stimulus, wherein the analysis computationally extracts data from the image, which data represents features characterizing the hepatocytes; and
- (b) classifying, with the computational device, the stimulus by quantitatively evaluating the extracted data which represents features to identify one or more hepatotoxic pathologies resulting from the stimulus, wherein the computational device is configured to classify at least two hepatotoxic pathologies selected from the group consisting of pathology classifications include two or more of the following: necrosis, cholestasis, steatosis, fibrosis, apoptosis, and cirrhosis.
- 2. (Original) The method of claim 1, further comprising, prior to analyzing the image: exposing a hepatocyte culture to the stimulus; and imaging the hepatocytes to produce the image.
- 3. (Previously presented) The method of claim 2, wherein multiple hepatocyte cultures are located on a single support structure, and wherein each *in vitro* culture is exposed to a distinct stimulus.
- 4. (Original) The method of claim 3, wherein at least two of the cultures are exposed to different quantities of the same stimulus.
- 5. (Original) The method of claim 3, wherein the support structure is a glass or plastic support.
- 6. (Original) The method of claim 3, wherein hepatocytes are co-cultured with support cells.
- 7. (Original) The method of claim 1, wherein the stimulus is exposure to a chemical compound.
- 8. (Original) The method of claim 1, wherein the hepatocytes are transformed or immortalized cells.

- 9. (Original) The method of claim 8, wherein the transformed or immortalized cells have been modified to express one or more cytochrome P450 metabolizing enzymes.
- 10. (Original) The method of claim 1, wherein analyzing the image comprises segmenting the image to identify individual hepatocytes on the image.
- 11. (Currently amended) The method of claim 1, wherein the features represented by the data extracted in (a) comprise two or more of features selected from the group consisting of membrane permeability, enzyme activity, Golgi distribution, migration of cytochrome c from the mitrochondria, mitochondrial membrane potential, condensation, fragmentation and granularization of nuclei, accumulation of lipid containing vacuoles, bile production, actin morphology, and tight junction condition.

12-19. Cancelled

- 20. (New) A computational method of assessing the hepatotoxicity of a stimulus, the method comprising:
- (a) segmenting, with a computational device, an image of hepatocytes that have been exposed to a stimulus in order to identify individual hepatocytes on the image;
- (b) extracting data from the segmented image, which data represents features characterizing the hepatocytes; and
- (c) classifying, with the computational device, the stimulus by quantitatively evaluating the extracted data which represents features to identify one or more hepatotoxic pathologies resulting from the stimulus,

wherein the computational device is configured to classify at least two hepatotoxic pathologies selected from the group consisting of necrosis, cholestasis, steatosis, fibrosis, apoptosis, and cirrhosis; and

wherein the data extracted in (b) represents at least one feature selected from the group consisting of membrane permeability, enzyme activity, Golgi distribution, migration of cytochrome c from the mitrochondria, mitochondrial membrane potential, condensation, fragmentation and granularization of nuclei, accumulation of lipid containing vacuoles, bile production, actin morphology, and tight junction condition.

- 21. (New) The method of claim 20, further comprising, prior to obtaining the image: exposing a hepatocyte culture to the stimulus; and imaging the hepatocytes to produce the image.
- 22. (New) The method of claim 21, wherein multiple hepatocyte cultures are located on a single support structure, and wherein each *in vitro* culture is exposed to a distinct stimulus.
- 23. (New) The method of claim 22, wherein at least two of the cultures are exposed to different quantities of the same stimulus.
- 24. (New) A computational method of assessing the hepatotoxicity of a stimulus, the method comprising:
- (a) analyzing, with a computational device, an image of hepatocytes that have been exposed to a stimulus, wherein the analysis computationally extracts data from the image, which data represents features characterizing the hepatocytes; and
- (b) classifying, with the computational device, the stimulus by quantitatively evaluating the extracted data which represents lipid and/or cytoskeletal features to identify one or more hepatotoxic pathologies resulting from the stimulus, wherein the computational device is configured to classify at least two hepatotoxic pathologies selected from the group consisting of necrosis, cholestasis, steatosis, fibrosis, apoptosis, and cirrhosis.
- 25. (New) The method of claim 24, further comprising, prior to analyzing the image: exposing a hepatocyte culture to the stimulus; and imaging the hepatocytes to produce the image.
- 26. (New) The method of claim 25, wherein multiple hepatocyte cultures are located on a single support structure, and wherein each *in vitro* culture is exposed to a distinct stimulus.
- 27. (New) The method of claim 26, wherein at least two of the cultures are exposed to different quantities of the same stimulus.